



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

P.0705

Antidepressant response prediction by early response, prefrontal theta cordance in rapid-eye movement sleep and ABCB1 genotype

T. Mikoteit¹, D. Spieker¹, C.K. Staeuble², H.E. Meyer zu Schwabedissen², A. Steiger³, M.A. Zeising³, M. Hatzinger¹

¹Psychiatric Services of Solothurn and University of Basel, Clinic for Psychiatry- Psychotherapy and Psychosomatics, Solothurn, Switzerland; ²University of Basel, Department of Pharmaceutical Sciences, Basel, Switzerland; ³Max Planck Institute of Psychiatry, Sleep endocrinology, Munich, Germany

Background: Prefrontal theta cordance in rapid-eye movement sleep (PTC-R) is a marker of the medial prefrontal activity and a promising biomarker for treatment response of major depression [1,2]. Further, from a clinical point of view, early treatment response at week 1-2 is also an acknowledged predictor of treatment response at week 4-6 [3]. Moreover, there is evidence that polymorphisms of the gene ABCB1 (rs2032583, rs2235015) which encodes the drug transporter P-glycoprotein (P-gp) could be involved in antidepressant (AD) treatment response, depending on whether the AD is substrate or non-substrate of P-gp [4,5]. The aims of this prospective clinical study were to evaluate 1) if the biomarker PTC-R and the clinical finding of "early response" at week one are independent from each other, 2) if the combination of both indicators lead to a better prediction of treatment response at week 5 and 3) if a match between ABCB1 genotype and substrate status of AD distinguishes between treatment responders and non-responders. **Methods:** Twenty-three in-patients with major depressive episodes (age: 42.2 ± 12.8 years, 52.2 % females) were included in the study at treatment onset with antidepressants. Experts rated the depression severity with the Hamilton Depression Rating Scale (HAMD) at baseline, at week 1, and at week 5. Early response was defined as a $\geq 20\%$ reduction of baseline HAMD at week 1, final response was defined as a $\geq 50\%$ reduction of baseline HAMD score at week 5. The PTC-R was assessed with a sleep EEG at week 1. The genotypes for both polymorphisms of the ABCB1 transporter gene (rs2032583, rs2235015) were determined retrospectively, and AD were assigned to substrate or non-substrate status to P-gp according to [5]. The combination of a high P-gp activity and a substrate AD were defined as mismatch, whereas a combination of a low P-gp activity and a substrate AD or any genotype and a non-substrate AD were defined as match.

Results: PTC-R and early response did not correlate with each other ($r_s = 0.29$, $p = 0.17$). According to a binary logistic regression analysis, early response predicted final response significantly ($\chi^2 = 10.45$, $p = 0.001$), while PTC-R marginally reached the significance level ($\chi^2 = 3.32$, $p = 0.068$). The combination of both indicators improved the prediction by PTC-R alone (18.5 % vs. 55.6 % improvement of the prediction model, $\chi^2 = 8.55$, $p = 0.003$). A match between the ABCB1 gene variants and substrate status of AD medication did not improve the combined model ($\chi^2 = 1.83$, $p = 0.39$).

Conclusions: These preliminary results indicate that as early as at week one, both PTC-R and early response are capable to predict treatment outcome at week 5. The combination of both predictors seems to be more reliable, giving the opportunity to intervene at that early stage of treatment prospectively. Though a match between the ABCB1 genotype and AD substrate status is expected to facilitate drug response, selection of the AD according to match or mismatch to ABCB1 genotype seems to be less relevant.

No conflict of interest

References

- [1] Adamczyk, M, Gazea, M, Wollweber, B, Holsboer, F, Dresler, M, Steiger, A, Pawlowski, M, 2015. Cordance derived from REM Sleep-EEG as a biomarker for treatment response in depression - a naturalistic study after antidepressant medication. *J Psychiatr Res* 63, 97-104.
- [2] Pawlowski, MA, Gazea, M, Wollweber, B, Dresler, M, Holsboer, F, Keck, ME, Steiger, A, Adamczyk, M, Mikoteit, T., 2017. Heart rate variability and cordance in rapid eye movement sleep as biomarkers of depression and treatment response. *J Psychiatr Res* 92, 64-73.
- [3] Stassen, HH, Angst, J, Hell, D, Scharfetter, C, Szegedi, A., 2007. Is there a common resilience mechanism underlying antidepressant drug response? Evidence from 2848 patients. *J Clin Psychiatry* 68, 1195-1205.
- [4] Uhr, M, Tontsch, A, Namendorf, C, Ripke, S, Lucae, S, Ising, M, Dose, T, Ebinger, M, Rosenhagen, M, Kohli, M, Kloiber, S, Salyakina, D, Bettecken, T, Specht, M, Pütz, B, Binder, EB, Müller-Myhsok, B, Holsboer, F., 2008 Jan 24. Polymorphisms in the drug transporter gene ABCB1 predict antidepressant treatment response in depression. *Neuron* 57 (2), 203-209.
- [5] Holsboer, F., 2017. Clinical Impact of Pharmacogenetic Testing on Antidepressant Therapy. *Ann Depress Anxiety* 4 (1), 1085.

doi: [10.1016/j.euroneuro.2021.10.777](https://doi.org/10.1016/j.euroneuro.2021.10.777)

P.0707

Suicide attempt and depression after COVID-19 vaccination: a case report

I.A. Gencan, B.M. Özacar, Ş. Hun Şenol, M. Altıntaş

Istanbul Kartal Dr. Lütfi Kırdar City Hospital- Psychiatry Clinic, Psychiatry, İstanbul, Turkey

The coronavirus disease 2019 (COVID-19) pandemic is having a profound effect on all aspects of society, including mental and physical health [1]. Vaccines to prevent SARS-CoV-2 infection are considered to be the most promising approach for the pandemic and are being vigorously pursued [2]. Since the outbreak began, researchers around the world have been trying to develop vaccines for COVID-19, with more than 198 vaccines currently in preclinical or clinical development phase [3]. Inactivated SARS-CoV-2 vaccine (CoronaVac) is one of the vaccine that has been in use in Turkey. It has been on the market a while now and some adverse effects are defined but many others are waiting to be discovered. This article reports a case of prolonged fatigue, depression, loss of functionality and suicide attempt after the CoronaVac vaccination. The reported patient was

72 years old female and had no background of any psychiatric disorder. The patient was admitted to the emergency service after a suicide attempt by drug overdose. After the patient's observation was completed in the emergency service, psychiatric evaluation was performed. The patient had depressive mood, loss of joy, anhedonia, fatigue, psychomotor retardation, feeling of worthlessness and recurrent suicidal thoughts nearly everyday for a two months period. She received the first dose of CoronaVac vaccination on the 24th of February in 2021. After the first injection she developed nausea, vomiting, dizziness, fatigue and hypertension. A complete examination has been made in another hospital and any organic pathology has not been detected. Because of this symptoms, she was scared to get the second dose of vaccine. Fatigue, and other depressive symptoms increased and got worsened and she made superficial cuts with kitchen knife on the dorsal faces of both her ankles and wrists five days prior to suicide attempt. She took unknown amount of chlorpromazine that expired in 1970 to commit suicide. The patient was admitted to psychiatry clinic and after a treatment process with venlafaxine she discharged with her own will and depressive symptoms were in remission. The psychiatric background has been evaluated for the causes of depression such as recent stressor, trauma, loss of family members, life style changes or anxiety about the pandemic but any specific cause could not be found. In addition during this time the patient was not infected by COVID-19 virus. In previous studies the most common side effects caused by the CoronaVac were mild pain and redness at the injection site and slight fatigue [4]. But this study observed the participants only for 28 days, so prolonged side effects that may be caused by the CoronaVac has not been reported yet. Our patient is the first case reported that developed a fully depressive episode after CoronaVac vaccination. It may guide clinicians in establishing a linkage between prolonged fatigue and depressive symptoms in vaccinated patients.

No conflict of interest

References

- [1] Holmes, EA, O'Connor, RC, Perry, VH, et al., 2020. Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *Lancet Psychiatry* 7 (6), 547-560.
- [2] World Health Organization. Draft landscape of COVID-19 candidate vaccines. <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>. 2021
- [3] Zhang, Y, Zeng, G, Pan, H, et al., 2021. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis* 21 (2), 181-192.
- [4] Pu, J, Yu, Q, Yin, Z, et al., 2021. The safety and immunogenicity of an inactivated SARS-CoV-2 vaccine in Chinese adults aged 18-59 years: A phase I randomized, double-blinded, controlled trial. *Vaccine* 39 (20), 2746-2754. doi:10.1016/j.vaccine.2021.04.006.

doi: 10.1016/j.euroneuro.2021.10.778

P.0708

Cariprazine's role in major depressive disorder

R. Gasparinho, N. Fernandes, L. Ferreira, N. Santos, I. Costa, A. Alho, M. Martins, I. Costa

Hospital Distrital de Santarém, Department of Psychiatry and Mental Health, Santarém, Portugal

Background: Cariprazine, a novel antipsychotic, is a dopamine multifunctional agent acting as a partial agonist at dopamine and serotonin receptors. Cariprazine is approved for the treatment of schizophrenia, and acute treatment of manic or mixed episodes associated with bipolar I disorder. Cariprazine's role is currently being studied in the treatment of acute bipolar I depression and as an adjunctive treatment to antidepressant therapy in patients with treatment-resistant Major Depressive Disorder (MDD).

Objective: To review the current evidence on the use and safety of Cariprazine as an adjunctive treatment in patients with treatment-resistant MDD.

Methods: We did a naturalistic review through a Pubmed search with Mesh terms cariprazine", "Depressive Disorder", "Depressive Disorder, Treatment-Resistant" and "Depressive Disorder, Major". Search was restricted to articles written in English, without temporal limitation. Total of 17 results; 16 articles selected.

Results: Cariprazine is a potent Dopamine D3-preferring receptor partial agonist. It differs from other antipsychotics due to its partial agonist activity, to its higher affinity in vitro for D3 receptors when compared to D2 receptors, and due to the balanced occupation of D2 and D3 receptors in humans. Cariprazine is also a partial agonist of 5-HT1A receptors, has low affinity for 5-HT2B and for histaminergic H1 receptors. Cariprazine has no meaningful affinity for cholinergic muscarinic receptors. Cariprazine has two principal active metabolites, desmethyl-cariprazine (DCAR) and didesmethyl-cariprazine (DDCAR). Both metabolites have similar receptor activity and functional activity to its precursor, but DDCAR's half-life is substantially longer than that for Cariprazine and so it's DDCAR's systemic exposure.

Cariprazine has a low incidence of metabolic effects or weight gain, and sedation is not expected. It is not associated with clinically relevant alterations in ECG QT interval, it doesn't raise prolactin levels and, consequentially, sexual dysfunction is not expected. Cariprazine's most common reported adverse events were akathisia, insomnia and nausea. Compared to other antipsychotics, so far, Cariprazine has proven to be similarly effective and possibly better tolerated than some antipsychotics in terms of weight gain and sedation.

Through its action mechanisms Cariprazine plays an important role in motivation, reward-related behavior, cognition, anxiety and mood. Additionally, Cariprazine may enhance selective serotonin reuptake inhibitors (SSRIs) effects. It has already shown an antidepressant-like action in animal models. Clinical trials in humans so far have mixed and inconclusive results, but there is a clear tendency towards clinical efficacy in treatment-resistant MDD.